

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising an agent that specifically binds to an MAFA ligand on a target cell and prevents or inhibits NK- or T cell- expressed cell surface MAFA from binding to the MAFA ligand on the target cell, and a pharmaceutically acceptable excipient.

2. The pharmaceutical composition of claim 1, wherein preventing or inhibiting an NK- or a T cell-expressed cell surface MAFA from binding to the MAFA ligand on the target cell prevents or inhibits the cell surface MAFA from generating an inhibitory signal to the NK or the T cell.

3. The pharmaceutical composition of claim 2, wherein preventing or inhibiting the cell surface MAFA-generated inhibitory signal stimulates an NK cell or a T cell activity.

4. The pharmaceutical composition of claim 3, wherein the stimulated NK cell or T cell activity is an increase in NK cell- or T cell-mediated cell killing.

5. The pharmaceutical composition of claim 4, wherein the stimulated NK cell or T cell activity is an increase in NK cell or T cell-mediated tumor cell killing.

6. The pharmaceutical composition of claim 3, wherein the stimulated T cell activity is an increase in T killer cell (CTL) activity, an increase in CTL activity against virally infected cells or cytokine secretion by the T cell.

7. The pharmaceutical composition of claim 1, wherein the agent that specifically binds to the MAFA ligand on the target cell comprises a soluble MAFA polypeptide.

8. The pharmaceutical composition of claim 7, wherein the soluble MAFA polypeptide comprises the extracellular domain of a MAFA polypeptide.

9. The pharmaceutical composition of claim 7, wherein the soluble MAFA polypeptide is a human MAFA polypeptide.

10. The pharmaceutical composition of claim 9, wherein the soluble human MAFA polypeptide comprises a sequence from about amino acid residue 64 to about amino acid residue 189 of SEQ ID NO:1.

11. A kit comprising a pharmaceutical composition comprising

5 a soluble MAFA polypeptide capable of specifically binding to a MAFA ligand on a target cell, and a pharmaceutically acceptable excipient; and

printed matter comprising instructions for using the pharmaceutical composition to stimulate an NK cell or a T cell activity or to treat an NK cell- or T cell-susceptible tumor or to identify an NK or a T cell target.

10 12. The kit of claim 11, wherein the stimulated NK cell- or T cell- activity is an increase in NK cell- or T cell-mediated cell killing.

13. The kit of claim 12, wherein the stimulated NK cell- or T cell-activity is an increase in NK cell- or T cell-mediated tumor cell killing.

14. The kit of claim 11, wherein the stimulated T cell activity is an increase in T killer cell (CTL) activity, an increase in CTL activity against virally infected cells or cytokine secretion by the T cell.

15 15. A pharmaceutical composition comprising an agent that specifically binds to an NK- or a T cell- expressed cell surface MAFA and prevents or inhibits the NK- or T cell- expressed cell surface MAFA from binding to a MAFA ligand, and a pharmaceutically acceptable excipient.

16. A pharmaceutical composition comprising an agent that specifically binds to an NK- or a T cell- expressed cell surface MAFA and prevents or inhibits the NK- or T cell- expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell, and a pharmaceutically acceptable excipient.

17. The pharmaceutical composition of claim 16, wherein preventing or inhibiting the NK- or T cell- expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell, stimulates an NK cell or a T cell activity.

18. The pharmaceutical composition of claim 17, wherein the stimulated NK cell or T cell activity is an increase in NK cell or T cell-mediated cell killing.

19. The pharmaceutical composition of claim 18, wherein the stimulated NK cell- or T cell-mediated cell killing is an increase in NK cell or T cell-mediated tumor cell
5 killing.

20. The pharmaceutical composition of claim 17, wherein the stimulated T cell activity is an increase in T killer cell (CTL) activity or cytokine secretion by the T cell.

21. The pharmaceutical composition of claim 20, wherein the increase in T cell activity is an increase in T killer cell (CTL) activity against virally infected cells.

22. The pharmaceutical composition of claim 16, wherein the agent that specifically binds to the NK- or the T cell- expressed cell surface MAFA is an anti- MAFA
10 antibody.

23. A pharmaceutical composition comprising a subsequence of an anti-MAFA antibody as set forth in claim 22, wherein the subsequence comprises an antigen binding
15 site.

24. A kit comprising a pharmaceutical composition comprising an antibody or a composition comprising a subsequence of an anti-MAFA antibody, wherein the subsequence comprises an antigen binding site, that specifically binds to an NK- or a T cell- expressed cell surface MAFA and a pharmaceutically acceptable excipient,

20 wherein the antibody binding to the NK- or T cell-expressed cell surface MAFA prevents or inhibits the MAFA from generating an inhibitory signal to the NK or the T cell; and

printed matter comprising instructions for using the pharmaceutical composition, wherein the instructions indicate use of the pharmaceutical composition to stimulate an NK cell or a T cell activity.

25 25. The kit of claim 24, wherein the instructions indicate use of the pharmaceutical composition to increase NK cell or T cell mediated cell killing.

26. The kit of claim 25, wherein the instructions indicate use of the pharmaceutical composition to increase NK cell- or T cell-mediated tumor cell killing.

27. The kit of claim 24, wherein the instructions indicate use of the pharmaceutical composition to increase T killer cell (CTL) activity or to increase cytokine secretion by the T cell.

28. The kit of claim 27, wherein the increased CTL activity is an increase in CTL activity to virally infected cells.

29. A pharmaceutical composition comprising an agent that specifically binds to an NK- or a T cell- expressed cell surface MAFA to generate an inhibitory signal to the NK or the T cell, and a pharmaceutically acceptable excipient.

30. The pharmaceutical composition of claim 29, wherein generating the inhibitory signal to the NK or the T cell prevents or inhibits an NK cell or a T cell activity.

31. The pharmaceutical composition of claim 30, wherein the inhibited NK cell or T cell activity is a decrease in NK cell- or T cell-mediated cell killing.

32. The pharmaceutical composition of claim 30, wherein the inhibited T cell activity is an decrease in T killer cell (CTL) activity or cytokine secretion by the T cell.

33. The pharmaceutical composition of claim 30, wherein the inhibited NK cell or T cell activity is a decreased or inhibited allogenic response or graft or transplant rejection reaction or inhibition of an autoimmune reaction or disease.

34. The pharmaceutical composition of claim 29, wherein the agent that specifically binds the NK cell- or the T cell-expressed cell surface MAFA is an anti- MAFA antibody.

35. A kit comprising a pharmaceutical composition comprising an antibody that specifically binds to an NK- or a T cell- expressed cell surface MAFA, or a composition comprising a subsequence of an anti-MAFA antibody, wherein the subsequence comprises an

antigen binding site that specifically binds to an NK- or a T cell- expressed cell surface MAFA, and a pharmaceutically acceptable excipient,

wherein the antibody binding to the NK- or T cell-expressed cell surface MAFA generates an inhibitory signal to the NK or the T cell; and

5 printed matter comprising instructions for using the pharmaceutical composition, wherein the instructions indicate use of the pharmaceutical composition to inhibit an NK cell or a T cell activity.

36. The kit of claim 35, wherein the instructions indicate use of the pharmaceutical composition to inhibit an NK cell activity.

37. The kit of claim 36, wherein the inhibited NK cell activity is a decrease or inhibition of allogenic reactions or graft or transplant rejections or to inhibit autoimmune disease.

38. The kit of claim 36, wherein the instructions indicate use of the pharmaceutical composition to inhibit T killer cell (CTL) activity, to inhibit cytokine secretion by the T cell, to decrease or inhibit graft or transplant rejections, or to inhibit autoimmune reaction or disease.

39. A method for inhibiting an NK- or a T cell- expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps

(a) providing a soluble agent that prevents the binding of the NK- or the T cell-expressed cell surface MAFA to its target cell ligand; and

20 (b) contacting the soluble agent to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell.

40. The method of claim 39, wherein the soluble agent that prevents the binding of the NK- or the T cell-expressed cell surface MAFA to its target cell ligand is an anti-MAFA antibody, or a composition comprising a subsequence of an anti-MAFA antibody, 25 wherein the subsequence comprises an antigen binding site, that binds to the cell surface MAFA.

41. The method of claim 39, wherein the soluble agent that prevents the binding of the NK- or the T cell-expressed cell surface MAFA to its target cell ligand is a soluble MAFA polypeptide that binds to the target cell ligand.

42. The method of claim 41, wherein the soluble MAFA polypeptide
5 comprises the extracellular domain of a MAFA polypeptide.

43. The method of claim 41, wherein the MAFA polypeptide is a human MAFA polypeptide.

44. The method of claim 43, wherein the soluble human MAFA polypeptide comprises a sequence from about amino acid residue 64 to about amino acid residue 189 of SEQ
ID NO:1.

45. The method of claim 39, wherein the contacting is in vitro or ex vivo.

46. The method of claim 39, wherein the contacting is in vivo.

47. The method of claim 46, wherein the in vivo contacting comprises administering the soluble agent to a subject.

48. The method of claim 47, wherein the subject is a mammal.

49. The method of claim 48, wherein the mammal is a human.

50. The method of claim 39, wherein the target cell is a tumor cell.

51. The method of claim 39, wherein inhibiting the NK- or the T cell-expressed cell surface MAFA binding to the ligand on the target cell prevents or inhibits the NK-
20 or T cell- expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell.

52. The method of claim 51, wherein preventing or inhibiting the NK- or T cell- expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell stimulates an activity of the NK or the T cell.

53. The method of claim 52, wherein the stimulated NK cell or T cell activity is an increase in NK cell- or T cell-mediated cell killing.

54. The method of claim 53, wherein the stimulated NK cell- or T cell-mediated cell killing is tumor cell killing.

5 55. The method of claim 52, wherein the stimulated T cell activity is an increase in T killer cell (CTL) activity or cytokine secretion by the T cell.

56. The method of claim 55, wherein the stimulated T cell activity is an increase in T killer cell (CTL) activity against virally infected cells.

57. A method for treating a tumor by stimulating the cytotoxic activity of an NK cell or a cytotoxic T cell (CTL), wherein the tumor comprises an NK cell- or CTL-susceptible tumor cell, comprising the following steps:

10 (a) providing a soluble MAFA polypeptide that binds to a MAFA ligand expressed on the tumor cell or an antibody or a composition comprising a subsequence of an anti-MAFA antibody, wherein the subsequence comprises an antigen binding site, that binds to an NK- or CTL- expressed cell surface MAFA; and

15 (b) administering the soluble MAFA polypeptide or anti-MAFA antibody in an amount sufficient to prevent binding of the NK- or CTL- expressed cell surface MAFA to its ligand on the tumor cell and to stimulate the cytotoxic activity of the NK or T cell to the tumor cell.

20 58. A method for inhibiting an activity of an NK cell or a T cell comprising the following steps:

(a) providing a soluble agent that binds to an NK cell- or CTL-expressed cell surface MAFA; and

25 (b) administering the soluble agent in an amount sufficient to inhibit an activity of the NK cell or the T cell.

59. The method of claim 58, wherein the soluble agent comprises an antibody, or, a composition comprising a subsequence of an anti-MAFA antibody, wherein the subsequence comprises an antigen binding site, that binds to an NK- or CTL- expressed cell surface MAFA.

5 60. The method of claim 58, wherein the inhibited NK cell or T cell activity is cell killing by the NK cell or the T cell.

61. The method of claim 58, wherein inhibited NK cell or T cell activity delays or inhibits a graft or transplant rejection or an allogenic response or ameliorates an autoimmune disease.

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